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14. ABSTRACT

To date we have completed many of the milestones set forth in the proposal: 1) Hired and trained Graduate Research Assistants (GRA) in administration of neuropsychological measures (Task 1) and recruited subjects following approval of human subjects committee (Task 2). Further, throughout the project we consulted with C-SHOP on proper training and implementation of ANAM for validation of the VRCPAT. While our original ending date for the Period of Performance was 30 September 2011, there was a delay in protocol approval that led to delays in subject recruitment. We requested and received a 6 month extension. The tasks that remain to be completed include: 1) Development and coding of the data from the VRCPAT, ANAM, and paper-and-pencil analyses unto a coherent and consistent database for analyzing the data—including data analytics related to the three sets of measures (i.e., VRCPAT, ANAM, and paper-and-pencil) for psychometric validation (Task 3). 2) Preparation of data for publication (Task 4).

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INTRODUCTION:

Clinical neuropsychologists are being asked to make statements regarding a soldier's functional skills, ability to return to active duty, and competence in tasks of community living. These concerns are what are referred to by the term ecological. The changing referral questions bring up a critical issue: most neuropsychological tests are outdated paper and pencil administrations that were developed to detect, and attempt to localize, the presence of brain damage rather than to be ecologically sound. To date, research establishing the ecological validity of neuropsychological tests has been limited. Neuropsychological tests that were once validated for their ability to detect brain damage now must be evaluated for their utility as ecological instruments. Given the increasing prevalence of blast injuries to the head, and the fact that many brain injuries may have no external marker of injury, there is need for researching innovative assessment methods in detecting blast-related brain injury. Further, since such injuries can greatly interfere with the soldier's ability to perform complex cognitive and emotional processing tasks involved in optimal performance at work these assessments need to have ecological validity. Virtual reality (VR) is as an advanced computer interface that can allow a soldier to become immersed within a computer-generated simulation. Potential VR use in assessment and training of soldier cognitive processes is becoming recognized as technology advances. Since VEs allow for precise presentation and control of dynamic perceptual stimuli (visual, auditory, olfactory, gustatory, ambulatory, and haptic conditions), they can provide ecologically valid (i.e. military relevant) assessments that combine the veridical control and rigor of laboratory measures with a verisimilitude that reflects real life situations. Once the psychometric properties of these norm-based virtual reality measures of neuropsychological functioning are established, the Army would have a comprehensive, flexible and scalable VR assessment system that could be extended to investigate a substantial set of pragmatic military performance assessment questions.

BODY:

This study was designed as an initial validation of the VRCPAT in a military cohort. The University of Southern California and Madigan Army Medical Center's National Center for Telehealth and Technology are collaborating on an initial pilot study to validate the VRCPAT with active duty military personnel. We compared paper-and-pencil neuropsychological tests, ANAM, and VRCPAT on behavioral measures. While our original ending date for the Period of Performance was 30 September 2011, there was a delay in protocol approval that led to delays in subject recruitment. We requested and received a six month extension. The tasks that remain to be completed include: 1) Development and coding of the data from the VRCPAT, ANAM, and paper-and-pencil analyses unto a coherent and consistent database for analyzing the data—including data analytics related to the three sets of measures (i.e., VRCPAT, ANAM, and paper-and-pencil) for psychometric validation (Task 3); and 2) Preparation of data for publication (Task 4). Although we are currently furthering the work to develop all aspects of the data base (for example, incorporating the VRCPAT Humvee Stroop and the civilian cohort), we have completed initial analyses on the VRPASAT and VRPVSAT. Our primary hypotheses were: 1) the VRPASAT (but not the VRPVSAT) would be significantly correlated with the paper-and pencil PASAT; and 2) the VRPASAT and VRPVSAT would be correlated with ANAM subtests assessing mathematical processing and procedural reaction time.

Participants and Procedure:

A total of 49 (94% were male) military service members participated in the study. Fifty percent of participants had 3 years or less of military service experience, and years of experience ranged from 1 to 24 years. All participants were fluent English speakers and had normal or corrected to normal vision. Each participant gave informed consent prior to participation in this research study. After informed consent was obtained, basic demographic information was recorded. Next, participants were assessed on the PASAT; ANAM, VRPASAT, and VRPVSAT.

Paper-and-Pencil PASAT:

Each participant was presented with a series of single digit numbers, in which the two most recent digits must be summed. For example, if the digits "2", "6" and "3" were presented, the participant was to respond with the correct sums: "8" and then "9". Practice trials occurred prior to the first trial. Stimuli are presented at four different rates (2.4 s, 2.0 s, 1.6 s, and 1.2 s). The duration of each digit was approximately .4 s.

ANAM:

The following ANAM subtests were given in the order presented: TBI Questionnaire; Sleepiness Scale; Mood Scale; Simple Reaction Time; Code Substitution; Procedural Reaction Time; Math Processing; Matching to Sample; and Go/No-Go.

Middle Eastern City (VRPASAT):

While virtually ambulating through a Virtual Iraqi City, the participant was presented with the VRPASAT—a virtual reality variation of the traditional PASAT. After following a sergeant to 6 zones, the participant was tested on navigation and spatial memory by being instructed to turn around and find the way back through each of the zones in reverse order.

Middle Eastern Checkpoint (VRPVSAT):

An area of the Middle Eastern City has been constructed to resemble a traffic checkpoint with a variety of moving vehicles arriving, stopping and then moving onward into the city. Participants listened to a virtual trainee as the trainee classified passing vehicles. In between vehicle presentations, the user was exposed to visual PASAT stimuli. Herein the numbers are presented against an Iraqi checkpoint background.
Data Analytics

Correlations were run between the three types of PASAT, and the virtual reality based PASATs were also correlated with various tests from the ANAM. In particular, we were interested in the relationship of the participants' performance on the PASATs and the mathematical processing and procedural reaction time tests.

A separate set of analyses were conducted to assess differences in participants' performance on the various PASATs employed. A 3 (PASAT type) by 2 (session) repeated measures ANOVA was utilized to serve this purpose. Separate ANOVAs were employed to test differences between the virtual reality PASATs in comparison to the paper and pencil version during the first two sessions, and the second two sessions.

Results

Correlations between performance on the VRPVSAT and tests in the ANAM test battery revealed that VRPVSAT performance is correlated with mathematical processing, $r = 0.50$, $p < 0.001$, as well as performance on the procedural reaction time test, $r = 0.41$, $p < 0.01$. Likewise, the VRPASAT was also correlated with both mathematical processing, $r = 0.43$, $p < 0.01$, and procedural reaction time performance, $r = 0.47$, $p < 0.01$.

The correlation analysis involving all three PASATs revealed that the VRPASAT was correlated with the paper and pencil version of the PASAT, r ¬= 0.78, $p < 0.001$. The VRPVSAT and the paper and pencil PASAT were not significantly correlated, $r = 0.26$, $p = 0.07$.

The ANOVA involving all three PASATs and using the first two sessions of the paper and pencil PASAT (2.4 and 2.0 respectively), evidenced a main effect of PASAT type, $F(2, 47) = 72.54$, $p < 0.001$, such that the highest performance was found during the VRPVSAT as a paired-samples t-tests revealed that performance was

significantly higher than performance on both the VRPASAT, $t(48) = 11.60$, $p < 0.001$, and the paper and pencil PASAT, $t(48) = 3.43$, $p < 0.01$. The VRPASAT was the most difficult task as performance was significantly higher on the paper and pencil PASAT, $t(48) = 11.12$, $p < 0.001$. A session main effect was also revealed, as performance on the first session was higher in general, $F(1, 48) = 39.84$, $p < 0.001$. The interaction between PASAT type and session was also significant, $F(2, 47) = 10.76$, $p < 0.001$, due to the lack of a significant difference in performance from session 1 to session 2 in the VRPVSAT. The ANOVA utilizing the third and fourth sessions of the paper and pencil PASAT (1.6 and 1.2 s respectively) evidenced the same main effect and interaction results. However, the difference between performance on the paper and pencil and VRPASAT was no longer significant, $t(48) = 0.452$, $p = 0.65$.

Discussion

The Checkpoint VRPVSAT and the City Walkthrough VRPASAT were correlated with both mathematical processing and procedural reaction time. These results are consistent with the view that the PASAT measures speed of information processing; mathematical ability, and attention.

Participant performance on the City Walkthrough VRPASAT had a strong positive correlation with performance on the paper and pencil PASAT, demonstrating high levels of convergent validity between the two tests. Differences in performance between the two PASATs were evidenced during the first two sessions of the paper and pencil PASAT, but not during the second two, more difficult, sessions. This result may be explained by the fact that the City Walkthrough VRPASAT includes the secondary memory task as well as the added distracting environmental stimuli. Thus, even when the interstimulus interval involved is longer during the virtual reality based PASAT, the task is more difficult due to other stimuli requiring cognitive resources. The City Walkthrough VRPASAT may also allow for more variability in performance without adding to participant frustration by speeding up the test.

As hypothesized, the VRPVSAT and the paper and pencil PASAT were not significantly correlated. These results are consistent with the studies using various patient groups (e.g., TBI; and multiple sclerosis) that have found PVSAT performance to be superior to PASAT performance. This superior visual performance is typically interpreted as representing an "interference" framework, in which the articulation of the response aurally interferes with the aural presentation of the digits. Hence, less interference exists between incoming visual stimuli and the articulated response on the VRPVSAT than on the VRPASAT. As a result, VRPVSAT may proffer a more robust measure of speed of information processing.

Future work should assess the clinical validity of the VRPASAT and VRPVSAT in a clinical population. Although further validation with an intact civilian population is needed, assessment of the difference between the VRPASAT and VRPVSAT may have important clinical implications.

KEY RESEARCH ACCOMPLISHMENTS:

Quarter 1:

- Meetings with Dr. Gilliland's team and Dr. Parsons's NeuroSim Lab at USC/ICT. Discussed the various stimuli and metrics needed for an executive function task (e.g., Stroop) being embedded in a virtual reality environment (e.g., Humvee) with safe and ambush zones
- IRB and other military review submitted
- Meeting with Dr. Reger at Madigan Army Medical Center. He is currently working on getting a cohort together for military selection of participants
- Also had meeting with Dr. Stetz at Tripler Army Medical Center…focus upon extending potential applicant pool
- Developed a manual and have trained psychometrists to administer and score VRCPAT

- Identified appropriate programmer to make changes to virtual environment per discussions with C-SHOP (Gilliland) and MAMC (Reger)
- Working with programmer to make changes to virtual environment per discussions with C-SHOP (Gilliland) and MAMC (Reger)
- Had additional meeting and send release to Dr. Stetz at Tripler Army Medical Center…focus upon extending potential applicant pool
- Develop some data output resources for the Virtual Reality Based Stroop task and potential use of psychophysiological metrics.

QUARTER 2:

- Meetings with Dr. Gilliland's team and Dr. Parsons's NeuroSim Lab at USC/ICT.
- Discussed the data analytics necessary for scoring and analyzing data relative to various stimuli and metrics.
- Developed scoring rubrics and data base structure.
- Developed codebook.

QUARTER 3:

- Worked with Human Subjects Protection Scientist Sarah L. Donahue, PhD, MPH, CIP from the Human Research Protection Office to make sure data transfer from Ft. Lewis Madigan Army Medical Center met U.S. Army Medical Research and Materiel Command requirements
- Further developed and programmed the scoring for the VRCPAT metrics to make sure that they comport well with C-SHOP version of related tests
- Worked with Ft. Lewis/Madigan Army Medical Center to discuss the preliminary database development and the necessary aspects of de-identification.
- Developed a template for the database that Ft. Lewis/Madigan Army Medical Center will populate and send to TATRC
- Sent an example database to Ft. Lewis/Madigan Army Medical Center so that they can see a preferred approach to structuring the database

QUARTER 4:

- Worked with Ft. Lewis/Madigan Army Medical Center to develop the database. After multiple iterations, we have developed a database that represents the structure necessary for data analytics
- Received data from Madigan and began the process of sorting the data and developing the appropriate scoring algorithms
- Worked with C-SHOP to make sure that we had all the data necessary for cross validation of the VRCPAT with ANAM-- Adjusted data to be better analyzed using scoring programs (e.g., Matlab)
- Performed a number of scoring conversions and conventions to the data base to make sure that we have both primary cognitive score metrics and constraint analyses
- Performed preliminary analyses comparing the virtual reality-based serial assessment tests (VR paced auditory serial assessment test; and VR paced visual serial assessment test) with standard paper and pencil PASAT and various ANAM computerized tests (described above).
- Note: Worked with Mr. Lance Nowell to develop and implement a no cost extension. Received a six month "No Cost Extension" (see Appendix).

REPORTABLE OUTCOMES:

- Presented "Virtual Reality in Cognitive Assessment and Return to Duty" to the TATRC sponsored Review and Analysis Workshop: Methods and Metrics for the Biological Assessment of Brain Dysfunction. May 24-25, 2011. Georgetown Conference Center. Washington, DC
- Manuscript submitted to Medicine Meets Virtual Reality

CONCLUSION:

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Future work should assess the clinical validity of the VRPASAT and VRPVSAT in a clinical population. Although further validation with an intact civilian population is needed, assessment of the difference between the VRPASAT and VRPVSAT may have important clinical implications. Over the next six months, we will be continuing our efforts at developing and coding the data from the VRCPAT, ANAM, and paper-and-pencil analyses unto a coherent and consistent database for analyzing the data—including data analytics related to the three sets of measures (i.e., VRCPAT, ANAM, and paper-and-pencil) for psychometric validation (Task 3). Further, during the next several months we will be preparing manuscripts for publication.

REFERENCES:

None at this time.